



Environmental Knights of the Roundtable

The Roundtable on Environmental Health Sciences, Research, and Medicine can be thought of as a think tank—a neutral, nonofficial setting where scientists, government officials, academics, industry representatives, and members of advocacy groups can gather to consider and discuss new scientific findings and emerging issues in environmental health. The roundtable, based at the Institute of Medicine (IOM) in Washington, D.C., is purposefully deliberative in nature. Its 34 members do not recommend specific actions or provide formal advice.

Despite that policy, the group has become highly influential in helping to shape the research agenda for fields in

are forming that weren't there, and it's out of that kind of stirring the pot that something like the roundtable can produce enormous benefits," she says.

Roundup in Houston

The roundtable has instituted a series of regional meetings across the nation. With its inherent neutrality, the roundtable seeks to facilitate dialogue among often-contentious groups in these regional meetings. "So often, these are individuals who only see each other in an adversarial setting," says Goldman. "So it's got to be healthy for people to be brought together in a setting where they can listen to

each other, where they're not directly at odds, where they're not litigating each other, where they're not fighting about what's going to be in a regulation."

Following on successful regional meetings in Pittsburgh and Atlanta, the roundtable began 2004 with a January 23 conference in Houston. Like the two previous venues, the city and its surrounding region present a unique

environmental situation, and a community atmosphere that the roundtable felt would be conducive to its message. "I often say Houston is ground zero for the interplay between many economic and environmental issues," says Myron Harrison, senior health advisor for ExxonMobil Corporation and a roundtable member. "Houston has very real challenges. It's a very business-oriented, high-growth, internationally oriented city. It won't be able to achieve the growth and stature that is envisioned if it is difficult to attract new business and highly educated employees. Accomplishing this is in part dependent upon solving a broad set of air, land, and water issues."

Goldman elaborates: "[Houston is] a place where there's a very sharp interface between the human imprint on the land and the natural environment, a natural environment that's fairly fragile. On top of that, there is a tremendous diversity in that community, with enormous issues of environmental empowerment, environmental justice, and social equality. All of that came to the fore in the workshop."

Jane Laping, executive director of the local environmental group Mothers for Clean Air, was pleased that the roundtable chose to come to Houston. "It's nice to finally be recognized," she says. "We're the fourth largest U.S. city, we've got the largest petrochemical complex here, we've got the worst ozone in the country for the fourth year now—it's pretty bad. We really need some help."

The one-day Houston workshop featured presentations on the many pressing environmental health issues in the



Texas town meeting. The roundtable met in Houston to examine the region's environmental health issues.

its purview. It has also helped what some observers felt was a disparate, fractured discipline to define itself more clearly and more broadly. By articulating a more holistic approach to environmental health, incorporating the natural, social, and built environments, the roundtable seeks to expand the dialogue, encouraging collaborations and partnerships among stakeholders. By identifying potential approaches to deal with new challenges, the group seeks to enhance the effectiveness of environmental health research and medicine in improving and protecting public health. "We try to find approaches toward making a contribution that would be unique to a body like the roundtable," says NIEHS deputy director and roundtable member Samuel Wilson.

Roundtable workshops are designed to educate participants so that they can make informed decisions in their own arenas, whether they come from federal or state agencies, industry, or academia. The regional meetings are intended not only to provide information about regional environmental issues and concerns, but also to serve as outreach mechanisms, allowing local stakeholders to learn about new approaches while interacting with each other in the neutral roundtable setting.

Roundtable co-chair Lynn Goldman, a professor of environmental health sciences at the Johns Hopkins Bloomberg School of Public Health, finds the group's many forms of interaction to be exciting and valuable. "Suddenly there's an 'a-ha' in the room, where connections and collaborations

region, including air pollution, water quality and flooding problems, urban sprawl, and obesity, as well as material on potential solutions such as sustainable growth, green buildings, and the importance of partnerships. "No one group, no one sector, no one set of stakeholders is going to solve anything by themselves," says Harrison. "It only happens when you get these partnerships. . . . And we showed some good examples of partnerships at the Houston meeting."

Wilson agrees that the Houston conference was successful in that regard. "There have been some significant follow-up activities that look very positive," he says. "The scientists have become involved with the civic planners, also the environmental groups have made contact with the academics much more effectively as a result of the meeting. And it seems that the whole community down there is working on this topic in a much more tangible, enthusiastic, and robust way than it had before."

The roundtable also held a regional meeting in Iowa in November 2004 (after this article's press time) to examine the state of health and the environment in rural areas of the state.

Emerging Issues: Nanotechnology

With the rapid development of nanotechnology, the roundtable felt the time was right to examine the potential environmental health issues involved with the expected proliferation of nanomaterials into virtually every aspect of commerce in the coming decades. By encouraging increased attention and research on the possible health and environmental pitfalls presented by nanomaterials, the roundtable hopes to contribute to the growing efforts among many stakeholders to maximize the enormous anticipated benefits of the technology by discovering and minimizing its associated risks.

The workshop, Technology and Environmental Health: Implications of Nanotechnology was convened in Washington, D.C., on 27 May 2004. Although many nanotechnology conferences have been held recently, Goldman says this one was different, thanks to the nature of the round-

table's proceedings: "We were able to provide a neutral ground for discussion, and be able to hear from science leaders who are right at the cutting edge of doing toxicological assessments, leaders of industry who are right at the cutting edge of developing products, social science and policy experts who've been looking at the issue, and the people who are leading the nanotech efforts in the government."

Presentations covered the gamut of issues related to nanotechnology, from potential applications in medicine and environmental remediation to potential health risks, along with discussions about societal implications and the importance of public perception to the technology's ability to deliver on its promises. Ultimately, the meeting served as a forum for consideration of research needs in the area, to ensure that environmental health questions are answered before it's too late to prevent negative impacts.

Says Christine Coussens, program officer of the IOM Board of Health Sciences Policy and study director of the roundtable: "The real purpose was to find out what's missing in terms of a research agenda as the technology is developing."

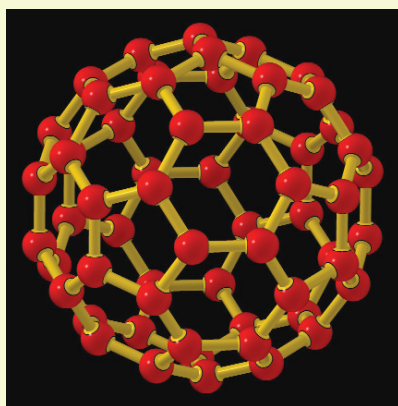
Goldman feels that the mix of attendees and the timing of the

they usually have, an audience that was very, very important in terms of bringing together the leadership from the federal health agencies. I was very pleased . . . that the meeting was able to be influential at a time that's very critical."

A Meeting of the Minds on Disasters

On 22 June 2004, the roundtable held Public Health Risks of Disasters: Building Capacity to Respond, its first workshop in collaboration with another IOM group, the Disasters Roundtable. The conference was staged with the intent of integrating expertise and ideas from the two disciplines as well as increasing the role of public and environmental health considerations in disaster response. "The idea actually came from an internal request at the National Academies," says Coussens. "The Disasters Roundtable hadn't been spending a lot of their time talking about health and health risks associated with disasters. They knew a lot about disasters—infrastructure, communications, and other facets—and we knew a lot about health, and so we were asked to put together a workshop agenda that would look at some of the cross-cutting issues, trying to integrate between the two disciplines."

Presenters at the meeting included emergency preparedness officials from the Department of Homeland Security and the Department of Health and Human Services, along with the director of the Centers for Disease Control and Prevention, public health and disasters experts from academia, and emergency management officials from both large and smaller metropolitan areas. With both natural and terrorism-related disasters seemingly inevitable, workshop participants stressed the need for enhanced collaboration and coordination among all those involved in disaster preparedness and response. They also advocated expanding preparation, mitigation, and response efforts to include hospitals, health care professionals, non-governmental organizations, mass media, private businesses, academia, and the engineering and scientific communities. Many presentations



Balancing buckyballs. A workshop on nanotechnology looked at both the potential benefits and the potential dangers to health.

meeting were both fortuitous: "There's a small group of experts in nanotechnology, and a number of them were on the agenda, but I think they had a different audience than



Chance favors the prepared. A workshop on disasters brought new perspectives to the thinking on preparedness and response planning.

explored the impacts of disasters on public health, including topics such as rapid assessment of health effects during disasters, infrastructure loss as a public health risk, and health effects of terrorism.

Roundtable member Jack Azar, who is vice president of environment, health, and safety at Xerox Corporation, was particularly anxious that the private sector be included in more multidisciplinary, integrated preparedness and response planning. "I was the only person from industry who spoke," he says, "and what I asked was for industry to be included in the kinds of discussions that go on in emergency preparedness situations normally between government and nongovernment organizations [such as the Red Cross] only. One hundred million people are usually in the workplace when these things happen, so businesses really need to be brought into it as well."

According to Goldman, the conference succeeded in increasing communication between the two fields. "I think this kind of meeting enriches the tools you have in your toolbox for doing things like assessing and managing risk, and hopefully helps to identify areas where more research,

more information would be valuable for protection of the population. There's more to it than screening your bags at the airport."

Spanning the Globe

With the next roundtable workshop, Global Environmental Health in the 21st Century: From Government Regulation to Corporate Social Responsibility, held 13–14 October 2004 in Washington, D.C., the group



Industrial evolution. The move from government regulation to corporate social responsibility was debated at a recent roundtable workshop.

turned its attention to globalization as a potential driver of environmental health. Many companies in the United States are actually multinational, and they're governed under a number of different countries' regulations, says Coussens. One major question for the symposium was how this impacts environmental health in the United States and globally.

The initial thrust of the workshop was the concept of environmental management systems, the organized programs by which companies ensure adherence to high standards of environmental stewardship. For many companies, the concept is embodied in certification by the International Organization for Standardization under ISO 14001, an environmental management system that has been adopted around the world. But there is controversy over the effectiveness of such standardized approaches. "It's not clear how environmental management systems impact or help to minimize the impact on environmental health," says Azar. "There hasn't really been any work trying to look scientifically at the impacts, what the benefits have been of [companies] getting ISO 14001-certified."

Environmental regulation was another major theme. Several industry representatives pointed out the challenges brought about by the increasing global diversity of regulatory approaches. "Twenty years ago, the United States had [environmental regulation] to itself," says Harrison. "It set the regulations, and then everyone copied them. That's no longer the case. . . . These days, the leading edge of regulation is in the European Union [EU]. The EU is much more aggressive."

Industry is increasingly seeing what could be characterized as a globalization of environmental regulation, as multinational companies respond to requirements imposed by different countries. "What's happening is you're getting different regulatory regimes created," explains Harrison, "but for these companies that operate all around the world, you can't be developing one product for one country and one product for another country—they have to do it all the same." This will be a fertile

Headliners

NIEHS-Supported Research

Neurological Disease

area for future research, as scientists investigate the impact of such globalization on environmental health.

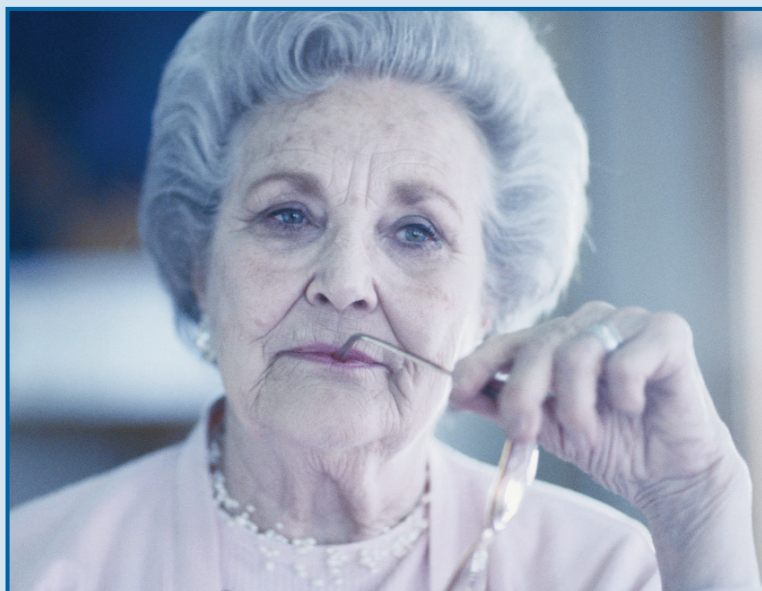
Many companies are now moving beyond regulatory compliance to embrace a concept called corporate social responsibility, and the potential impact of that trend was very much on the workshop's agenda. Today, says Harrison, companies are faced not just with health and safety expectations, nor just with environmental expectations, but also with a long list of what are called social indicators, which include biodiversity, fair labor practices, and human rights. "The corporate social responsibility agenda is driving every bit as much activity—and maybe more in some places and some companies—than is regulation," he says.

Azar concurs: "Everybody understands we've got to go well beyond compliance to a more sustainable concept. But it can be defined in many different ways. It's going to take a different form whether you're a chemical company, an electronics company, an appliance company, or an automobile company." The workshop included presentations from both advocates and skeptics of voluntary corporate responsibility measures. The workshop, says Coussens, also raised awareness of the transparency that is needed to ensure corporate social responsibility. "It's got to be more than some kind of marketing gimmick," she says. "It has to provide real, useful data."

Wilson anticipates this workshop will have long-term ramifications for the field of environmental health. "Integrating industrial practices into environmental health more so that there's a much better communication pathway between the two groups is very important, and I think there's a lot of downstream work to do on that," he says.

The roundtable had an ambitious agenda in 2004, and the future looks to be equally challenging. As the scope of the roundtable expands, it is likely that its influence upon the field of environmental health will continue to grow, as will its success in providing a unique forum for consideration of the many complicated issues it faces. —Ernie Hood

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Neural Protein May Stop the Progression of Alzheimer Disease

Stein TD, Anders NJ, DeCarli C, Chan SL, Mattson MP, Johnson JA. 2004. Neutralization of transthyretin reverses the neuroprotective effects of secreted amyloid precursor protein (APP) in APPSW mice resulting in tau phosphorylation and loss of hippocampal neurons: support for the amyloid hypothesis. *J Neurosci* 24:7707–7717.

As many as 4.5 million Americans suffer from Alzheimer disease (AD), which usually begins after age 60, and the risk of developing the disease goes up with age. About 5% of men and women aged 65–74 have AD, and nearly half of those aged 85 and older have the disease.

AD is characterized by the presence of protein plaques and tangles of fibers in brain tissue. The disease may in fact be caused by the abnormal processing of the so-called amyloid precursor protein and the accumulation of the protein β -amyloid. Other brain abnormalities in people with AD include nerve cell death in specific areas that are vital to memory and other mental abilities, as well as lower levels of certain neurotransmitters. A recent study by NIEHS grantee Jeffrey Johnson of the University of Wisconsin–Madison has identified a protein known as transthyretin that blocks the effects of β -amyloid.

In working with a transgenic mouse containing defective human genes associated with early-onset AD, Johnson and colleagues noticed that although these mice had high levels of β -amyloid, they did not exhibit any neurodegenerative symptoms. Further investigations led the team to discover that these mice also were producing high levels of transthyretin. When the mice were given antibodies that prevented transthyretin from interacting with the β -amyloid protein, the mice showed typical brain cell death. *In vitro* studies of human brain cells treated with transthyretin and β -amyloid showed minimal amounts of cell death, confirming the results seen in the mice.

These studies show that transthyretin may block the progression of AD by inhibiting the effects of β -amyloid. This discovery suggests that it may be possible to develop a drug that increases the production of transthyretin and thus protects people at risk for AD, such as those with a genetic predisposition. The findings may also improve the chances of detecting potential environmental factors in the development of AD by allowing scientists to identify agents that upset the balance between transthyretin and β -amyloid proteins. —Jerry Phelps

Environmental Roots of Asthma

From 1980 to 1999, the number of U.S. doctor's office visits for asthma jumped from about 6 million to nearly 12 million, according to data from the Centers for Disease Control and Prevention, and the World Health Organization estimates cases worldwide at 100–150 million. Epidemiologic studies have linked the disease to a plethora of modern lifestyle factors, but the traditional focus has been on heredity and a few identifiable triggers such as animal dander, fungi, ozone, and pollens. At an October 2004 symposium titled *Environmental Influences on the Induction and Incidence of Asthma*, cosponsored by the NIEHS and the U.S. Environmental Protection Agency, presenters reviewed the scientific evidence for a wider expanse of predisposing factors, including environmental tobacco smoke (ETS) exposure, obesity,

asthma incidence. Of pivotal interest, from a developmental perspective, is how, why, and when some people acquire immunological tolerance to common allergens, while others go on to develop asthma.

"The programming of this tolerance begins during prenatal and postnatal development," said Harald Renz, a research scientist at Germany's Marburg University. In studies of traditional farm environments in Switzerland, Austria, and Germany, Renz's



Cats and clouds. Animal dander and secondhand tobacco smoke were just two environmental triggers of asthma discussed at a recent meeting cosponsored by the NIEHS and the EPA.

dietary fat intake, oxidative stress, and *in utero* xenobiotic exposures. The emerging array of dynamic interactions between genes, allergens, and pollutants all point to a complex profile of susceptibility and to new possibilities for public health intervention.

Acquiring a Healthy Tolerance

The critical interactions between genetic susceptibility and environmental exposures in the induction of asthma are likely to be heavily influenced by the developmental phase at which the exposures occur. For example, it has long been suspected that decreased exposure to microbes during early life may be contributing to the rise in

team consistently found an inverse relationship between asthma rates and maternal blood levels of the bacterial endotoxin lipopolysaccharide (LPS), which is a marker for exposure to gram-negative bacteria common in farmyards. "Infants born to mothers who maintained their daily farm work during pregnancy were almost completely protected from asthma," he said. "Animal studies using LPS during gestation have confirmed these findings: the offspring are large-

ly protected against the development of allergic inflammation and respiratory hyperresponsiveness."

Other investigators urged caution against overly simplistic perspectives on the protective impact of early-life exposures to microbes. "The focus on microbial exposure is only one piece of a much larger picture," said Peter Sly, a lung specialist at the Telethon Institute for Child Health Research in Perth, Australia. "Throughout early life, the immune system takes maturational cues from the environment in the form of microbial stimulation, bowel flora, mother's milk, and dietary factors. At the same time, the infant is exposed to allergens

in the diet and environment. If the allergen exposure coincides with those normal maturational cues, then you're less likely to develop allergic sensitization and asthma."

An Eye on Inflammation

In western societies, however, said Sly, maturational cues are often missing due to factors such as more sanitary living conditions and use of antibiotics. Problems arise, moreover, when the fetus or infant is exposed to airborne pollutants such as ETS and diesel exhaust particles (DEP), which can cause airway inflammation and may enhance allergic sensitization and drive disease expression. Increased protection against asthma therefore stems from a confluence of early-life microbial exposure, normal immune maturation, and low exposure to airway irritants or inflammatory factors.

The concept of synergy was a repeated theme at the symposium. One prominent example was the interaction between ragweed pollens and DEP, which have received increasing attention as culprits in the rising incidence of asthma. "Many studies have found that DEP enhances airway responsiveness in asthmatics," said clinical immunologist Andre Nel of the University of California Medical School in Los Angeles. "We also know that DEP has an adjuvant effect on the Th2 cytokine responses [specific immune responses that increase allergic tendencies] to ragweed pollens, causing an allergen-specific IgE response in humans and thus greater susceptibility to asthma."

Nel has studied the quinones, nitrogen oxides, and other pro-oxidative chemicals in DEP. These chemicals tend to increase oxidative stress and stimulate inflammatory pathways that, in turn, pave the way for asthma. Conversely, thiol antioxidants have been shown to interfere with the effects of DEP. Research is now needed to determine whether antioxidant treatment may be beneficial for children living along roadways with increased traffic density, where asthma prevalence tends to be higher.

Maritta S. Jaakkola, a senior scientist at the Institute of Occupational Medicine of England's University of Birmingham, reported on several studies showing a strong relationship between the extent of smoke exposure and asthma. Jaakkola's research has shown that prenatal, infant, childhood, and adult exposures can all predispose individuals to asthma. In a study in Finland, 8% of asthma cases that started in adulthood were attributable to ETS exposure within the preceding year. "Exposures to ETS in prenatal life, early childhood, and adulthood can all raise the risk of asthma," said Jaakkola. "For adults, even quite recent exposures can make a difference."

Different groups of mechanisms seem to be involved: ETS may promote chronic respiratory infections in early life, contributing indirectly to asthma risk. In contrast, ETS-related irritants that inflame the airways may play a stronger role in adult cases of asthma. Obese adults might also be at greater risk, given data presented by Stephanie Shore of the Harvard School of Public Health showing increased inflammatory cytokine levels and airway hyperresponsiveness in these individuals.

Additional discussions focused on the identification of inflammatory markers that can serve as potential indicators of asthma risk. Karin Yeatts, a researcher at the University of North Carolina Center for Environmental Medicine, Asthma, and Lung Biology, spearheaded a study on the effects of different particle sizes and their impact on inflammatory markers in adult asthma patients. Preliminary results indicate

that a subgroup of the asthmatic adults had increased levels of inflammatory markers in their lungs in response to increases in ambient concentrations of particles smaller than 2.5 microns. "The levels of particulate matter triggering the upper airway responses were actually lower than those specified by the current national regulations," said Yeatts. "This suggests that a subgroup of asthmatic adults who show this diverse spectrum of inflammatory cytokines in their blood may be at greater risk where the rest of the population would be relatively safe."

The symposium yielded a number of suggestions for public health interventions to lower asthma incidence. Among the proposed strategies were "healthy home" design and building remediation to minimize humidity and improve indoor air quality; changes in infection control to curb rising asthma rates in the elderly; increased education on maternal smoking as a preventable

risk factor; more green belts in urban areas as pollution buffers; stricter sanctions on emissions from automobiles and diesel engines, mandating diesel particle traps; a large-scale shift away from fossil fuel use; greater efforts to reduce exposures to known sensitizers in the workplace (including a ban on smoking at work); and better public health communication to all high-risk groups.

The public health challenge of asthma will call for a confluence of scientific and policy directives. "Ultimately, in tackling the problem of factors associated with asthma incidence, we are facing a new challenge to understand the complexity in host-environment interactions as well as the practical issues in developing social policy," said presenter Kevin B. Weiss, a professor of medicine at Northwestern University. "The challenge is great, but the potential for public health impact is even greater." —M. Nathaniel Mead

Building Blocks of Learning beyond the BENCH

Playing with blocks has long been a favorite pastime of children and one that parents often encourage as a means of developing reasoning, spatial acuity, and other skills. A program developed by the Community Outreach and Education Program (COEP) of the Massachusetts Institute of Technology (MIT) Center for Environmental Health Studies turns this childhood pastime into an effective method for teaching students about DNA and cellular processes by building models out of LEGO blocks.

Now a commercial product, the LEGO Life Science kits contain different-colored blocks representing the basic structural elements of DNA. So far, the kit series includes models of DNA, chromosomes, and photosynthesis. The kits were developed by Lexington public school teacher Kathleen Vandiver to bring the form and function of the double helix alive for middle-school students. Vandiver later joined the staff of the MIT COEP and has worked with the program to design a learning activity for students based on the kits called "The Shape of Life: From Helix to Chromosome."

The activity begins with students identifying LEGOs that represent molecules of sugar, phosphates, and nucleotide bases. Using these pieces, they construct their own twisting model of the DNA ladder, with careful attention to base pairing. A brief overview of DNA replication follows, using the LEGO DNA structure as a simulation aid. Students then have individual exploration time to answer

questions and investigate variations of their DNA model. Teachers may also add a mutation lesson.

Next, the students learn how DNA's complex sequence is replicated prior to mitosis, and the lesson scales up to the LEGO

Chromosomes kit to model the process of mitosis. The activity concludes with the study of structural components of chromosomes, including a discussion of genes and traits. With the Chromosomes kit, students can build a LEGO fish as a model to demonstrate how genes can be expressed in a living creature. The fish has only 3 chromosome pairs, rather than a human's 23 pairs, so it's easier to understand the relationship between genes and traits. Chromosomes, cell membranes, and spindle fibers are modeled in LEGOs as the students move through the stages of interphase, prophase, metaphase, anaphase, and telophase.

The kits can be used to teach many levels of students. Although originally designed for middle schoolers, they can be

reassembled into a more advanced version for use at the college level. Several introductory biology classes at MIT have used the sets. Says Vandiver, "It is important to realize that many people need to be taught the basics in order to understand the issues in environmental health." And what could be more basic—or fun—than playing with blocks?

The LEGO Life Science kits are available for purchase at <http://www.legoeducationstore.com/>. —Amy Fitzgerald



Constructive thinking. COEP researcher Luke Higgins (second from left) helps students build a DNA double helix from LEGOs.